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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE wpy

Office Action Summary	Application No.	Applicant(s)	
	09/977,261	ULLRICH ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,20 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,20 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group III, claims 14, 15 and 20 drawn to MKK1 protein in Paper No. 11 (7/18/03) is acknowledged. In addition, Applicant has elected SEQ ID NO: 2. Applicant did not distinctly and specifically point out any errors in the restriction requirement. Thus, the election has been treated as an election without traverse (MPEP§818.03(a)).

Applicant has added claim 31. Thus, claims 14, 15, 20 and 31 are pending. Claims 1, 2, 7, 10, 11, 23, 26, 29 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11 (7/18/03). The requirement is still deemed proper and is therefore made FINAL.

Specification

2a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

2b. The abstract of the disclosure is objected to because the abstract is in two paragraphs. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14, 15, 20 and 31 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3a. Claim 14 is rejected as being vague and indefinite in the recitation of the term "an isolated recombinant MKK1". Applicant has not indicated if it is the recombinant protein or the nucleotide is claimed.

3b. Claim 15 is rejected as being vague because amino acid sequence which depicts MKK1 is in Figures 1A, 1B and 1C (See 06/07/02 Submission). In addition, CRF indicates SEQ ID NO: 2 to illustrate the protein sequence (see also claim 31).

3c. Claims 14 and 20 are rejected as being vague and indefinite in the recitation of the term "MKK1 protein". The protein of interest is described by an arbitrary protein name. Applicant describes in the specification (see page 9, lines 30-35) that MMk1 could be from any species, in naturally occurring-sequence or in variant form, or from any source, whether natural, synthetic or recombinant. Thus, making the claims indefinite. It is unclear from which vertebrate species the nucleic acid encoding the said protein was isolated or what the identifying characteristics of MKK protein are. Applicant should particularly point out and distinctly claim the MKK1 by claiming it using sufficient structural characteristics associated with the protein (e.g. amino acid sequence, molecular weight, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 14 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses MKK1 polypeptide of SEQ ID NO: 2. This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose all the MKK1 polypeptides. The specification does not define what is meant by the generic term "MKK1" and discloses a single example. There is no description of what makes a MKK1 polypeptide a MKK1, any MKK1 from other species, or anything else that would be considered a "MKK1". In addition, the name "MKK1" encompasses mutant and modified MKK1 that are not described in the specification. The claims as written, therefore, encompass polypeptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph. The specification does not provide written to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of MKK1 polypeptide sequence of SEQ ID NO: 2, the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptide sequences, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the MKK1 polypeptide of SEQ ID NO: 2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed is not representative of the genus because the genus is unclear and potentially highly variant. As a result, it does not appear that the inventors were in possession of the scope of polypeptide sequences set forth in claims 14 and 20.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

4b. Claims 14 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on all polynucleotide molecules encoding MKK1 protein. However, other than MKK1 polypeptide sequence of SEQ ID NO: 2, the specification as filed fails to disclose any other nucleotide sequences. Applicant describes the polypeptde sequence from a single species (human) yet contemplates the MKK1 from other species, in naturally occurring –sequence or in variant form, or from any source, whether natural, synthetic, or recombinant. The lack of description of the various MKK1 forms in the specification does not enable one of skilled in the art make and/or use the invention.

Despite knowledge in the art for producing homologues of a given protein with nucleotide deletions, insertions or subtitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function of the protein. Furthermore, detailed information regarding the structural and functional

requirements of the disclosed protein is lacking. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990; Ngo et al., 1994).

Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which homologues would retain the functions of the protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of nucleotide sequences encompassed by the invention of claims 14 and 20. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claims 14 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Bennett et al. (1994, Ref. A6) or Sakano et al. (1994, Ref. A47).

Instant invention is directed to MKK1 (megakaryocyte kinase) proteins. Also described is a fusion protein.

Bennett et al. disclose the DNA and amino acid sequences of matk (megakaryocyte-associated tyrosine kinase) protein of megakaryocytic lineage (see abstract and Fig. 1). Sakano et al. teach the DNA and amino acid sequences of HYL (a non-receptor tyrosine kinase) from human megakaryoblastic cell line (see abstract and Figure 1). Like MKK1 of the present application, the disclosed proteins (matk and HYL) are nonreceptor tyrosine kinases of megakaryocytic lineage. Although, the disclosed proteins are not called MKK1, the amino acid sequences of the disclosed proteins are identical to SEQ ID NO: 2 of the presently claimed MKK1 (see Appendix A). Accordingly, they are the same product. Therefore, the disclosure of Bennett et al. or Sakano et al. anticipates claims 14 and 15.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7a. Claims 20 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (1994) or Sakano et al. (1994) in view of Maniatis et al. (1982, pages 422-430: Ref A37).

Instant invention is directed to MKK1 (megakaryocyte kinase) proteins. Also described is a fusion protein.

Teachings of Bennett et al. and Sakano et al. have been described above. However, neither Bennett et al. nor Sakano et al. teach a fusion protein comprising matk or HYL (MKK1) linked to a heterologous protein or peptide sequence. Maniatis et al. teaches expression of fusion proteins and discloses vectors suitable for expression of

fused eukaryotic proteins (pages 422-430). Maniatis also discusses the advantage of fusion proteins, such as stability in bacteria (page 422).

Accordingly, it would have been obvious to the skilled artisan to modify the matk or HYL protein of Bennett et al. or Sakano et al. by fusing it to a heterologous protein by the following the method of Maniatis, with the expectation of success of obtaining a high yield of the matk or HYL protein from *E.coli.* The motivation to obtain matk or HYL fusion protein is provided by Maniatis who discloses the advantages of fusion proteins. Therefore, the instant claims are *prima facie* obvious over Bennett et al. (1994) or Sakano et al. (1994) in view of Sambrook et al. (1982).

8. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER
9/30/03